Title: Factor V Leiden Thrombophilia *GeneReview* Supplemental Information: The p.Arg334Thr Variant and the p.Arg334Gly Variant
Author: Kujovich JL
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Note: The following information was provided by the author listed above and has not been reviewed by *GeneReviews* staff.

Two different variants at the p.Arg334 APC cleavage site have been reported, only one of which is associated with APC resistance.

The p.Arg334Thr variant in the APC cleavage site (factor V Cambridge) was identified in a British individual with a history of thrombosis and APC resistance in the absence of the Leiden variant [Williamson et al 1998]. Codon 334 is the second of three sequential APC cleavage sites in the factor V molecule. The same variant was found in the individual's mother, who also had an abnormally low APC resistance value. However, it was not found in 600 other individuals presenting with thromboembolism or in a population of normal blood donors, suggesting that it is a very rare factor V variant.

The p.Arg334Gly variant, a different variant in the same codon predicting an Arg-to-Gly substitution at position 334 in factor V, was identified in two of 43 Chinese individuals with a history of thrombosis and one control individual [Chan et al 1998]. This variant was not associated with APC resistance in the one individual tested with a coagulation screening assay. However, in a recombinant system, the factor V Cambridge variant and this variant showed identical APC resistance patterns with ratio values intermediate between those of wild type factor V and factor V Leiden [Norstrom et al 2002]. Another study found this variant in 4.7% of Hong Kong Chinese individuals, but did not identify it as a risk factor for thrombosis [Liang et al 1998].

Although the available evidence suggests that the p.Arg334Thr and p.Arg334Gly variants alone are not major risk factors for thrombosis, they may contribute to thrombosis risk when combined with other genetic or acquired risk factors. There are anecdotal reports of double heterozygosity for factor V Cambridge and the Leiden variant or the prothrombin 20210G>A variant in individuals with VTE [Santamaria et al 2005, Jeanne-Yvonne et al 2006].

References

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